REMARKS/ARGUMENTS

The foregoing amendment is of formal nature. Prior to the amendment, Claims 11-16 are pending and under examination. After the amendment, Claims 11, 13, 15 and 16 have been amended. The amendment is fully supported by the claims and specification originally filed and does not introduce any new matter. Applicants reserve the right to pursue the canceled subject matter in a continuation, continuation-in-part, and divisional application.

Specification

The Examiner objects to the title is not descriptive. Applicants have amended the title to recite "Anti-PRO220 Antibodies" The objection is thereby rendered moot.

Drawings

The Examiner asserts that Applicants have not submitted any drawings yet.

Applicants disagree and submit that the drawings were submitted in the original PCT/US04/26249 as Appendix A.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 11, 13 and 16are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention, for making reference to a figure.

The amendment of Claims 11, 13 and 16 renders the rejection to these claims moot.

Claim Rejection Under 35 U.S.C. §§101 and 112, First Paragraph

Claims 11, 13 and 16 are rejected under 35 U.S.C. §§101 and 112, first paragraph, as allegedly not supported by either a specific or substantial utility. The Examiner alleges that neither the specification nor the art discloses any specific disorders that will be affected by PRO220. (Page 8 of the instant Office Action). Applicants respectfully disagree for the reasons outlined below.

A. The Legal Standard for Utility

According to 35 U.S.C. §101:

> Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title. (Emphasis added).

In interpreting the utility requirement, in *Brenner v. Manson,*[1] the Supreme Court held that the quid pro quo contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent Applicant disclose a "substantial utility" for his or her invention, *i.e.,* a utility "where specific benefit exists in currently available form."[2] The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy."[3]

Later, in *Nelson v. Bowler,*[4] the C.C.P.A. acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a specific therapeutic use. The Court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."[5]

In *Cross v. Iizuka,*[6] the C.A.F.C. reaffirmed *Nelson*, and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of *in vivo* test results,

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[1] *Brenner v. Manson,* 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

[2] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

[3] *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

[4] *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

[5] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

[6] *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

i.e., there is a reasonable correlation there between."[7] The Court perceived, "No insurmountable difficulty" in finding that, under appropriate circumstances, "*in vitro* testing, may establish a practical utility."[8]

The case law has also clearly established that Applicants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face.[9] The Examiner has the initial burden that Applicants' claims of usefulness are not believable on their face.[10] In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."[11, 12]

Compliance with 35 U.S.C. §101 is a question of fact.[13] The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration.[14] Thus, to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the Applicant. The issue will then be decided on the totality of evidence.

The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines"),[15] which acknowledge that an invention complies with the utility

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[7] *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

[8] *Id.*

[9] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[10] *Ibid.*

[11] *In re Langer*, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (C.C.P.A. 1974).

[12] *See also In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (C.C.P.A. 1977).

[13] *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983) *cert. denied,* 469 US 835 (1984).

[14] *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d (BNA) 1443, 1444 (Fed. Cir. 1992).

[15] 66 Fed. Reg. 1092 (2001).

requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that are to be diagnosed.

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an Applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "'substantial'" utility.'"[16] Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement,[17] gives the following instruction to patent examiners: "If the Applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

B. Proper Application of the Legal Standard

Applying the above legal standard, Applicants respectfully disagree with this rejection and submit that, contrary to the Examiner's allegation, the specification provides specific and substantial utility for the claimed method.

1. The specification has provided specific utility for the claimed antibodies

Applicants submit that, contrary to the Examiner's assertion, the specification clearly indicates the specific conditions that can be diagnosed with the claimed antibodies, that is **immune-related diseases or inflammatory related diseases**. The asserted utility, diagnosis of immune-related or inflammatory related diseases, is specific to the subject matter claimed and provide well-defined and particular benefit to the public.

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[16] M.P.E.P. §2107.01.

[17] M.P.E.P. §2107 II(B)(1).

As stated in M.P.E.P. §2107.01, "a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the invention, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. *Knapp v. Anderson*, 477 F.2d 588, 177 USPQ 688 (CCPA 1973)."

Applicants in the present application identified that PRO220 of the present invention are differentially expressed in isolated activated CD4+ T cells as compared to isolated resting CD4+ T cells. This biological activity is specific and reasonably correlates with immune-related diseases. Thus, the asserted utility is falls into the category which are sufficient to identify a specific utility for the invention.

In addition, Applicants have identified in the specification various types of immune-related diseases that may be diagnosed with the presently claimed methods, for example, systemic lupus erythematosis, rheumatoid arthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis (scleroderma), idiopathic inflammatory myopathies (dermatomyositis, polymyositis), Sjogren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria), autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated thrombocytopenia), thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis), diabetes mellitus, immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis), demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barre syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease (ulcerative colitis: Crohn's disease), gluten-sensitive enteropathy, and Whipple's disease, autoimmune or

immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft-versus-host-disease. Infectious diseases including viral diseases such as AIDS (HIV infection), hepatitis A, B, C, D, and E, herpes, etc., bacterial infections, fungal infections, protozoal infections and parasitic infections. (see paragraph 2554).

The Examiner appears to take a position that the asserted diagnostic use must be limited to a single type of immune-related disease in order for meet the requirement of "specific utility." This position is incorrect since neither law nor the utility guideline prohibits a patentable invention from having multiple utilities. On the contrary, the fact that PRO220 may be involved in multiple types of immune-related disease exactly demonstrates that this molecule has important and specific "real world" clinical use.

2. *The specification has provide substantial utility for the claimed methods*

Applicants respectfully submit that the asserted diagnostic use has a significant and presently available benefit to the public because the specification provides sufficient support for the association of PRO220 and immune-related diseases.

In particular, Applicants have shown that various PRO polypeptides of the present invention are differentially expressed in isolated CD4+ T cells activated by ICAM-1 and anti-CD28 as compared to isolated resting CD4+ T cells. As described above, these data demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more immune disorders, but also serve as therapeutic targets for the treatment of those immune disorders. The overexpression was detected via microarray assay, a technology well-known in the art at the effective filing date of the present application.

As indicated in the "Background of the Invention," T lymphocytes (T cells) are an important component of a mammalian immune response. T cells recognize antigens which are associated with a self-molecule encoded by genes within the major histocompatibility complex (MHC). The antigen may be displayed together with MHC molecules on the surface of antigen

presenting cells, virus infected cells, cancer cells, grafts, etc. The T cell system eliminates these altered cells which pose a health threat to the host mammal. T cells include helper T cells and cytotoxic T cells. Helper T cells proliferate extensively following recognition of an antigen-MHC complex on an antigen presenting cell. Helper T cells also secrete a variety of cytokines, *i.e.,* lymphokines, which play a central role in the activation of B cells, cytotoxic T cells and a variety of other cells which participate in the immune response. CD4+ T cells are known to be important regulators of inflammation. Herein, CD4+ T cells were activated and the profile of genes differentially expressed upon activation was analyzed. As such, the activation specific genes may be potential therapeutic targets. *In vivo* co-stimulation is necessary for a productive immune proliferative response. The list of costimulatory molecules is quite extensive and it is still unclear just which co-stimulatory molecules play critical roles in different types and stages of inflammation. Knowing that PRO220 is overexpressed in the activated T cell, a skilled artisan would recognize that PRO220 is associated with immune-related diseases and can be used as a diagnostic marker for immune-related diseases.

Applicants submit that, as discussed above, the PR220 polypeptides have utility in the diagnosis of inflammatory-related or immune-related diseases. Based on such a utility, one of skill in the art would know exactly how to use the claimed method for diagnosis of immune-related diseases, without any undue experimentation.

Accordingly, Applicants respectfully request reconsideration and reversal of the enablement rejection of Claims 11-16 under 35 U.S.C. §§101 and 112, first paragraph.

Claim Rejection Under 102(b)

Claims 11-16 are rejected under 102(b) as being anticipated by Hillman *et al.* (2001), allegedly because Hillman discloses a polypeptide that is 100% identical to PRO220, as well as antibodies that bind to the polypeptide and pharmaceutical composition thereof.

Claim 11 has been amended by adding a limitation of "wherein said antibody modulates activity of T cells." Since Hillman does not disclose the association between PRO220 and immune-related diseases or activity of T cells, Hillman does not teach each and every element of amended Claim 11 and therefore does not anticipate Claims 11-16.

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **50-4634** (referencing Attorney's Docket No. **GNE-0267 R1 / 123851-181682**).

Respectfully submitted,

Date: October 23, 2009

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